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EXAMINER	
OLSON, ERIC	
ART UNIT	PAPER NUMBER
1623	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,142	MISTRETTA ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *11-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/12/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's amendment and arguments submitted September 3, 2008 wherein claims 3, 4, and 31 are amended. This application claims benefit of provisional application 60/442154, filed January 22, 2003, and claims priority to foreign application FR0300488, filed January 17, 2003.

Claims 1-31 are pending in this application. Claims 11-29 are withdrawn from consideration.

Claims 1-10, 30, and 31 as amended are examined on the merits herein.

Applicant's amendment, submitted September 5, 2008, with respect to the rejection of instant claim 4 for a minor grammatical error, has been fully considered and found to be persuasive to remove the objection as the grammatical error has been corrected. Therefore the objection is withdrawn.

Applicant's amendment, submitted September 5, 2008, with respect to the rejection of claim 3 under 35 USC 112, second paragraph for indefinitely reciting the terms "conventional amination method" and "simple shoulder", has been fully considered and found to be persuasive to remove the rejection as the indefinite terminology has been deleted from the claim. Therefore the rejection is withdrawn.

The following rejections of record in the previous office action are maintained:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5-7, 9, 10, 30, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Moreau. (US patent 6596861, of record in previous office action, previously published on September 21, 2000 as WO00/55210).

Moreau discloses methods for using microwave-assisted reactions to couple a polysaccharide to a polypeptide by reductive amination. (column 3, lines 18-50) Various reducing agents such as borohydride and cyanoborohydride can be used to reduce the imine linkage. (column 6 lines 44-51) Polypeptides useful in this method include capsular polysaccharides of *Streptococcus pneumoniae*, for example of serotype 5. (column 6 lines 58-61) The polysaccharides can be conjugated to various polypeptides including immune response enhancing polypeptides such as diphtheria and tetanus toxoids. (column 8, lines 27-36) This process of reductive amination without prior borohydride reduction is equivalent to the reductive amination protocol disclosed on p. 16, lines 10-17 and p. 34, example 1 in the instant specification which is used to produce a conjugate of structure II' according to claims 1, 2, 5-7, and 9. Therefore the structure of the resulting conjugate and its MNR and chromatographic properties are seen to be inherent properties of the *Streptococcus pneumoniae* type 5 conjugates disclosed by Moreau. Any properties exhibited by or benefits provided the composition

are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Therefore the claimed invention is anticipated by Moreau.

Response to Argument: Applicant's arguments, submitted September 9, 2008, with respect to the above ground of rejection, have been fully considered and not found to be persuasive to remove the rejection. Applicant argues that Moreau does not disclose a composition that necessarily possesses the level of purity of the claimed compositions. Specifically, Applicant argues that products made by the process mentioned in the claims would have undetectable levels of compound X contamination unlike compounds made by the method described by Moreau, which are never shown to be free of compound X. An aspect of the present invention is methods that avoid formation of compound X. According to Applicant's arguments filed September 6, 2008, "One method [of aminating the polysaccharide without forming compound X] comprises reductive amination in the presence of a reducing agent selective for a Schiff base for a period between 30 min. and 4 hours in a specific range of pH that is between 4 and 6.5, **longer periods of time resulting in the formation of the undesirable compound X**." Applicant further states that, "Moreau does not disclose such methods. Rather, Moreau combines microwaving with methods of amination that, **but for the duration of the amination**, are otherwise conventional." The specification as originally filed discloses

an inventive example (example 1, p. 34) that is typical of the claimed invention, wherein a pH 6.0 reaction buffer containing the type 5 polysaccharide , an amine, and sodium cyanoborohydride, is incubated at 50°C for 2 hours. The specification (p. 17 line 24 – p. 18 line 7) further discloses that the formation of undesirable byproducts is a function of time, with compound X being observed for incubation times of greater than 4 hours. Therefore it is observed that the critical element for suppressing the formation of compound X is in fact that the incubation time be no greater than 4 hours. By way of comparison, Moreau discloses that the reaction is carried out at the same temperature of 50°C for 15 minutes to 4 hours, with bacterial p[polysaccharides reacting to completion in as little as 15 minutes. (column 5 lines 42-55) Table 1 in column 11 shows that reaction of *Salmonella* type VI polysaccharide goes to completion in 15 minutes, and that undesirable degradation products are not formed over such a short incubation time. (column 11 lines 48-67) Therefore, given that Moreau teaches an incubation time that is in fact shorter than that of the claimed invention, the compositions produced by the method of Moreau will have a degree of purity at least as high as that of the instantly claimed compounds, including the absence of any compound X.

Applicant further argues that Moreau does not disclose any working examples of a process of aminating pneumococcus type 5 capsular polysaccharide. However, anticipation does not require the actual disclosure of working examples. It merely requires that the prior art contain adequate written description of the anticipated invention under the requirements of 35 USC 112. Moreau does in fact contain said written description, by describing the preferred reaction conditions and listing a number

of different bacterial capsular polysaccharides that can be aminated under these reaction conditions. Therefore Moreau does in fact teach an aminated capsular polysaccharide according to the instant claims.

Therefore the rejection is deemed proper and made **FINAL**.

The following rejections of record in the previous office action are maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moreau (US patent 6596861, of record in previous office action, previously published on September 21, 2000 as WO00/55210) in view of Jansson et al. (Cited in PTO-892)

It is noted that the ^{13}C NMR profile and chromatography profile of aminated pneumococcus type 5 capsular polysaccharide is claimed in the preamble of claims 1-4. In the aminated pneumococcus type 5 capsular polysaccharide claims, said profiles are considered to be inherent properties of aminated pneumococcus type 5 capsular polysaccharide, and therefore do not carry any patentable weight towards the claimed compound. Also, the method by which said compounds are produced does not have any patentable weight towards the claimed compound.

Moreau teaches a method for the reductive amination of polysaccharide useful in a process for conjugating polysaccharides to polypeptides (co1.1, lines 1-4). Moreau discloses the aminated capsular polysaccharide of Streptococcus pnemoniae of serotype 5 (col. 6, lines 60-61). Regarding claims 10, 30 and 31, the prior art discloses that the aminated polysaccharide can be conjugated to a polypeptide per se (co1.8, lines 60-61)'. Moreau also discloses the reductive amination of acidic (negatively charged) polysaccharide (co1.10, Example 1). Moreau discloses the pharmaceutical composition of said compounds and their conjugates thereof (co1.10, lines 24-29). The prior art is silent in disclosing the specific expanded formula which corresponds to pneumococcus type 5 capsular polysaccharide.

Jansson teaches the repeating-unit structure of Streptococcus pneumoniae type 5 capsular polysaccharide composed of glucose, N-acetylated fucosamine, N-acetylated pneumosamine (2-acetamido-2,6-deoxytalose), glucuronic acid and Sug (2-acetamido- 2,6-deoxyhexose-4-ulose) (page 101, abstract). Jansson discloses the ^{1}H and ^{13}C -NMR spectra characterizing the polysaccharide structure (page 103, fig. 1 and page 107). Jansson also discloses borohydride reduction of Streptococcus pneumoniae type 5 capsular polysaccharide to obtain the product having similar immunological activity, which can also be used as a vaccine, and suggests that this product would have a superior stability and reduced base-lability. (page 107, last para. to page 108, lines 1-3; page 108, last paragraph)

With regard to claims 5-9, wherein the repeating units are 90% and 95%; and A is represented by C=O or CHOH, it would be within the scope of the artisan in this art to

optimize them through routine experimentation of reductive amination of a polysaccharide in view of cited prior arts. Additionally, the at least 95% reduced product of claim 8 corresponds to the borohydride-reduced polysaccharides described by Jansson et al., while the structure of claim 9 where A is C=O corresponds to the non-borohydride-reduced polysaccharide prepared as described by Moreau without borohydride reduction.

It would have been obvious to person having ordinary skill in the art at the time the invention was made to produce conjugates of *S. pneumonidae* type 5 capsular protein with a carrier polypeptide by reductive amination according to Moreau et al., either with or without prior borohydride treatment, thus producing either conjugates of the A = CHOH structure II" or the A = C=O structure II', and to incorporate this conjugate into a pharmaceutical composition, such as a vaccine. One of ordinary skill in the art would have been motivated to produce these compounds and compositions because Moreau teaches a method for the reductive amination of polysaccharide useful in a process for conjugating polysaccharides to polypeptides; and Jansson teaches reduced Streptococcus pneumoniae type 5 capsular polysaccharide that has reduced degradation and browning on storage. The motivation is provided by Moreau, the prior art suggests that reductive amination of a polysaccharide of interest provides the product retaining essential antigenic determinants within the polysaccharides which is extremely important in the preparation of a conjugate vaccines having the essential structure and conformation of the component materials (col.2, lines 57-64). One of ordinary skill in the art would reasonably have expected success because the chemical

transformations described by Moreau and Jansson are well within the ordinary and routine level of skill in the art.

Therefore the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, submitted September 9, 2008, with respect to the above ground of rejection have been fully considered and not found to be persuasive to remove the rejection. Applicant's arguments are the same as those made against the rejection over Moreau alone with regard to the formation of the byproduct compound X, and are not found persuasive for the same reasons. Therefore the rejection is deemed proper and made **FINAL**.

Conclusion

No claims are allowed in this application. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Examiner, Art Unit 1623
11/25/2008

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623